

## Non-hodgkin lymphoma (NHL), epstein bar virus, progesterone receptor, and cross-talking: micro-environmental approaching of NHL as a new medical hypothesis

Ahed J Alkhatib

Jordan University of Science & Technology, Jordan, Email: [ajalkhatib@just.edu.jo](mailto:ajalkhatib@just.edu.jo)

### Abstract

This study explores non-Hodgkin Lymphoma from different perspectives. The present abstract introduces brief lymphomas, Epstein Bar Viruses (EBV), progesterone receptor, and the phenomenon of cross-talk.

Lymphomas start from harmful changes in lymphocytes, for the most part B cells. Immune system cells and NK cell inferred-lymphomas are less normal. The principal lymphoma type that was perceived is Hodgkin lymphoma (HL). The various lymphoma types have all been in all called non-Hodgkin lymphomas (NHL) and include different subtypes (like diffuse large B cell lymphoma, follicular lymphoma and small lymphocytic lymphoma) just as different T cell lymphomas (Swerdlow, 2008). According to Leak (2011), NHL ranks sixth most common cancer in the United States (US). From an epidemiologic point of view, NHL was mostly prevalent in some areas such as North America, Australia and Europe. On the other hand, the lowest rates were recorded in Asia and Pacific. It has been reported that 1 out of 110 men and 1 of 161 women are affected by NHL during their life span. However, increasing incidence of NHL may due to several factors such as lifestyle, demographic variables including age and gender, occupational conditions and environmental factors, infectious agents, genetics and family history, and autoimmune diseases (Farmanfarma et al., 2020).

NHL is classified into two main groups as either aggressive or non-aggressive (Hester et al., 2018). Examples of aggressive lymphoma include diffuse large B cell lymphoma (DLBCL), and follicular lymphoma (FL) is an example of non-aggressive lymphoma (Li et al., 2015). The disclosure of EBV was announced in 1964 (Lowe et al., 2019; Alkhatib, 2020). Around then, oncogenic infections were not pulling in the regard for be of clinical noteworthiness. Denis Burkitt's was the researcher who found this infection through assurance of the most widely recognized tumor in adolescence in Africa, while it was not known in the West (Ambinder, 2007). It was difficult for the academic network to concede the connection between EBV and BL. This issue took quite a long time to be acknowledged.

It is worth to make reference to those sero-epidemiologic examinations indicated that EBV was normal among different human populations (Alkhatib, 2020). The vast majority at the worldwide level are certain for EBV in the type of asymptomatic infection (Epstein et al., 1967; Hausen et al., 1970). It has been assessed that tumors due to infections speak to around 10% of disease frequency at worldwide level (Parkin, 2006; de Martel et al., 2012). EBV is known by its capacity for instigate infectious mononucleosis (IM). EBV has added with a few a wide range of diseases, including BL, hemophagocytic lympho histiocytosis, HL, gastric cancer and nasopharyngeal carcinoma (Maeda et al., 2009; Sherif et al., 2018). Progesterone receptor (PR) regulates biological activities of progesterone (Gadkar-Sable et al., 2005). PR is an individual from the nuclear/intracellular receptor superfamily of ligand subordinate interpretation factors (Tsai and O' Malley, 1994; Leonhardt et al., 2003). Following the interaction between progesterone and its receptor, a conformational change happens in PR. The receptor ligand complex is translocated to the core where it communicates with DNA restricting components in the genome and modifies the interpretation of progesterone- responsive qualities (Ismail et al., 2003). PR is an ace controller in female regenerative tissues that controls formative procedures and multiplication and separation during the conceptive cycle and pregnancy. PR additionally assumes a job in movement of endocrine-subordinate bosom malignancy. As an individual from the nuclear receptor group of ligand-subordinate interpretation factors, the primary activity of PR is to manage systems of target quality articulation because of restricting its related steroid hormone, progesterone (Grimm et al., 2016). Henson et al (2000) conducted a study using immunohistochemical techniques to evaluate the expression of estrogen receptor (ER) and progesterone receptor (PR) in 29 cases of equine lymphoma. Various types of lymphomas were included such as T-cell-rich large B-cell lymphomas, B-cell neoplasms, and T-cell lymphomas. Control cases were one normal equine lymph node. The results showed that ER was negative in cases and control samples. On the other hand, 55% of lymphoma cases were positive for PR. One case involving abdominal and thoracic tumors and leukemia was negative for PR expression. A low positivity for PR was observed in the normal lymph node.

The main aim of the present study was to explore how the previously mentioned elements in the tissue may interact together in initiating NHL (Alkhatib, 2018). In this context, Dolcetti (2015) pointed to the ability of EBV to modify the microenvironment to improve cell transformation. EBV has acquired the ability to improve the production of various factors to increase the growth and/or survival of lymphoid cells and to enable their escape from immune system reactions.

It is possible to think that progesterone in the tissues plays an important role in inducing pathologic cascades such as roles beyond its reproductive regulatory functions. The micro-environment within the tissue includes several components like pathogens and flora.

Viruses are also included taking into account their interactions with the host cellular mechanisms.

In this study, we suggest a new explanation of obesity and the increased prevalence of NHL. We recently reported that both HPV and CMV were localized in the adipose tissue of diabetic female rats. EBV is likely to be localized there (Alkhatib, 2020). In NHL, we previously reported that EBV binds PR in lymphoid cells as a matter of cross-talk. This finding is new and unique explaining NHL development.

Our proposed hypothesis implies the involvement of EBV, PR, and cross-talk in an integrating model to explain NHL occurrence. It is possible, but needs more in-depth studies to establish new therapeutic lines by interacting with these elements.

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